Ciba Specialty Chemicals Corporation
North America

Performance Polymers

8EHQ-0399-14408

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Ciba

MR 19924

March 9, 1999

CERTIFIED MAIL

Attn: Section 8(e) Coordinator
Document Processing Center (7407)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street, SW
Washington, D.C. 20460

8EHQ-99-14408

Re: TSCA Section 8(e) Notice: Acute Inhalation Toxicity in Rats

Ciba Specialty Chemicals claims no information in this letter as Confidential Business Information.

In accordance with the EPA policy statement and reporting guide on TSCA Section 8(e), Ciba Specialty Chemicals is submitting the enclosed recently received inhalation toxicity study of 4,4'-methylenedianiline bismaleimide (CAS Reg. No. 13676-54-5) in rats.

At an exposure levels of 1.6 mg/l/1hr., only one of 10 rats died. With subsequent testing at 1.9 mg/l/1hr. and 2.3 mg/l/4hrs., there were 5 out 10 and 9 out of ten deaths, respectively. In the two latter tests, some of the morbid and moribund animals showed some acute signs of neurotic toxic effects (ataxia and tremors), although this could have been the result of general overall toxicity of the test substance.

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You may contact me if there are any questions.

Sincerely,

Jonas Weiss

Dr. Jonas Weiss
Director, Product Safety

MR 19924

Enclosure: (1)

8esubmission

281 Fields Lane
Brewster, New York 10509

Tel. 914 785 3000

88990000127

Value beyond chemistry

MB Research Laboratories

1765 Wentz Road
P.O. Box 178
Spinnerstown, PA 18968
phone (215) 536-4110
fax (215) 536-1816

VOLUME I

Study Title	:	Acute Inhalation Toxicity in Rats/LC 50 in Rats
Test Article	:	MATRIMID 5292A US Batch #AG86890010
Author	:	Daniel R. Cerven, M.S., Study Director
Study Completed On	:	March 1, 1999
Performing Laboratory	:	MB Research Laboratories 1765 Wentz Road P.O. Box 178 Spinnerstown, PA 18968
MB Research Project #	:	MB 98-7240.05
MB Research Protocol #	:	318E-01
Sponsor	:	Ciba Specialties Chemical Corp. 281 Fields Lane Brewster, NY 10509
Citation	:	Daniel R. Cerven, M.S. (1998) Unpublished Report by MB Research Laboratories

Study Title : Inhalation Toxicity in Rats
Project # : MB 98-7240.05
Test Article : MATRIMID 5292A US
Batch #AG86890010
Protocol : 318E-01

GOOD LABORATORY PRACTICES STATEMENT

This study was conducted in accordance with the Good Laboratory Practices regulations of the EPA/FIFRA 40 CFR part 160 and TSCA 40 CFR 792, and the FDA, 21 CFR Part 58.

STUDY DIRECTOR :

Daniel R. Cerven, M.S. Date
MB RESEARCH LABORATORIES

PROJECT NUMBER	:	**MB 98-7240.05**
TEST ARTICLE	:	**MATRIMID 5292A US Batch #AG86890010**
SPONSOR	:	**CIBA SPECIALTIES CHEMICAL CORP.**
TITLE	:	**Acute Inhalation Toxicity in Rats/LC 50 in Rats**
PROTOCOL #	:	**318E-01**

A B S T R A C T

Objective: To provide information on health effects which may arise from short term exposure by the inhalation route. This study was designed to comply with the standards set forth by DOT 49 CFR 173.333 and was conducted in accordance with DOT Definitions 49 CFR 173.132.

Method Synopsis: Five healthy male and five healthy female Wistar Albino rats were exposed to an aerosol atmosphere of MATRIMID 5292A US Batch #AG86890010 at a concentration of 1.6 mg/l, for a period of one hour. Based on mortality occurring at this level, five males and five females were exposed to a concentration of 2.3 mg/l for a period of four hours. Based on mortality occurring at the 2.3 mg/l, five additional males and five additional females were exposed to a concentration of 1.9 mg/l for a period of one hour. Chamber temperature, relative humidity of air entering the chamber, chamber air flow and negative pressure were monitored and recorded. All rats were monitored during the exposure period, one hour after exposure and once daily thereafter for 14 days for toxicity and pharmacological effects. The rats were observed twice daily for mortality. Body weights were recorded prior to exposure, weekly and at death or termination in the survivors. All animals were examined for gross pathology. Abnormal tissues were preserved in 10% buffered formalin for possible future microscopic examination.

Concentration was estimated prior to exposure. Actual concentration was determined gravimetrically during exposure to be approximately 1.9 mg/l. Particle size analyses revealed a mass mean aerodynamic diameter of 6.97 with a geometric standard deviation of 2.77.

Summary: Mortality response to the inhalation exposures was:

Actual Concentration in mg/l	Exposure Period	# Exposed M/F	# Dead M/F
1.6	1 hour	5/5	1/0
1.9	1 hour	5/5	4/5
2.3	4 hours	5/5	4/5

A B S T R A C T

Summary (cont'd)

1.6 mg/l - One hour exposure - Nine of ten animals survived the one hour 1.6 mg/l exposure. One male died on day 1 with predeath physical signs of dyspnea, coating of the fur with test material and closed eyes. Necropsy revealed abnormalities of the lungs, eyes, liver, kidneys, adrenals and gastrointestinal tract, as well as wetness of the nose/mouth area.

Physical signs of abnormal licking, coating of the fur with test article and closed eyes were noted during the exposure period in the survivors. Instances of dyspnea and emaciation were noted in survivors during the remainder of the study. Body weight changes of survivors were normal in 5/9 survivors. Instances of weight loss were noted in four animals. Necropsy results of survivors were normal.

1.9 mg/l - One hour exposure - Five animals survived the one hour 1.9 mg/l exposure. Four males and one female died within 2 days of the exposure. Predeath physical signs included lethargy, ataxia, dyspnea, chromodacryorrhea, closed eyes, wetness and red staining of the nose/mouth area, and coating of the fur with test article. Necropsy revealed abnormalities of the lungs, nasal turbinates, eyes, pleural cavity, liver, kidneys and gastrointestinal tract, as well as red staining and wetness of the nose mouth area.

Physical signs noted in survivors included chromodacryorrhea, chromorhinorrhea, dyspnea, lethargy, piloerection, emaciation, tremors, sagging eyelids, coating of the fur with test article, closed eyes, hunched posture and wetness or red staining of the nose/mouth area. Body weight changes were normal in 4/5 survivors. One female lost weight during the study. Necropsy results were normal in 3/5 survivors and lung abnormalities were noted in two animals.

2.3 mg/l - Four hour exposure - One animal survived the four hour 2.3 mg/l exposure. Four males and five females died by day 1 with predeath physical signs of dyspnea, tremors, lethargy, sagging eyelids, piloerection, chromodacryorrhea, wetness and red staining of the nose/mouth area, fur coated with test article, closed eyes and abnormal climbing. Necropsy revealed abnormalities of the lungs, nasal turbinates, eyes, liver, adrenals and gastrointestinal tract, as well as wetness of the nose/mouth and anogenital areas.

Physical signs of dyspnea, lethargy, sagging eyelids, ataxia, flaccid muscle tone, red staining of the nose/mouth area, coating of the fur with test article and closed eyes, were noted in the surviving animal. Body weight changes and necropsy results of the survivors were normal.

Conclusion: The LC_{50} is approximately 1.9 mg/l. The test article is assigned to Packing Group II.

Study Title : Inhalation Toxicity in Rats
Project # : MB 98-7240.05
Test Article : MATRIMID 5292A US Batch #AG86890010
Protocol : 318E-01

OBJECTIVE

To provide information on health effects which may arise from short term exposure by the inhalation route. This study was designed to comply with the standards set forth by DOT 49 CFR 173.333 and was conducted in accordance with DOT Definitions 49 CFR 173.132.

TEST ARTICLE

Identity	:	MATRIMID 5292A US Batch #AG86890010
Source	:	Ciba Specialties Chemical Corp.
Date Received	:	11/12/98
Storage	:	The test article was stored at room temperature and humidity.
Description	:	White powder
Sample Preparation	:	Used as received

TEST DATES

Study Initiation	(date protocol signed)	:	11/18/98
Experimental Start Date	(1st exposure to test substance)	:	11/25/98
Experimental Term Date	(last date data collected)	:	01/05/99
Draft Report Signed	(if applicable)	:	02/11/99
Final Report Signed	(study completion)	:	03/01/99

EXPERIMENTAL DESIGN

Test Animals

Animals were received from Ace Animals, Boyertown, PA on 11/03, 11/10, 11/17, 12/01 and 12/15/98. Following a quarantine period of at least one week, fifteen healthy male and fifteen healthy, non-pregnant and nulliparous female Wistar Albino rats were selected for this test from a larger group.

The animals were born the weeks of 9/01 through 11/05/98. The pretest body weight range was 226 - 279 grams for males and 222 - 273 grams for females. Animals were identified by cage notation and indelible tail marks. The animals were housed 1/cage in suspended cages. Bedding was placed beneath the cages and changed at least three times/week. Fresh Purina Rat Chow (Diet #5012) and water were freely available except during the one hour exposure period. The animal room, reserved exclusively for rats on acute tests, was temperature controlled, had a 12 hour light/dark cycle and was kept clean and vermin free.

EXPERIMENTAL DESIGN (continued)

Dosing

Five male and five female rats were exposed to a 1.6 mg/l of MATRIMID 5292A US Batch #AG86890010, in an inhalation chamber for one hour. Based on mortality occurring at this level, five males and five females were exposed to a concentration of 2.3 mg/l for a period of four hours. Based on mortality occurring at 2.3 mg/l, five additional males and five additional females were exposed to a concentration of 1.9 mg/l for a period of one hour. Following exposure, animals were returned to individual housing and observed for 14 days.

Chamber Conditions (Appendices 1 & 2)

A 57 liter dynamic glass chamber designed to insure uniform spatial distribution of aerosols and which permitted continuous observation during exposure was used. The chamber was partitioned internally with wire screening into a total of ten non-restraining cubicles. One animal was placed in each cubicle. Chamber temperature and humidity of air entering the chamber were recorded. The airflow through the chamber was calculated to yield at least 10 to 15 air changes per hour so that adequate oxygen was supplied to the animals. The chamber was maintained at a negative pressure differential to the immediate environment in order to keep the test atmosphere contained. The temperature, humidity, airflow and negative pressure were recorded at approximately thirty minute intervals during the exposure period.

Generation

MATRIMID 5292A US Batch #AG86890010 was fed into a Venturi Dust Generator (Intox) via an augmented screw feeder. During the pretest concentration calibration phase, various screw feeder rates were used until the proper flow rate for generating each concentration was determined. The air flow in the Venturi tube creates suction at the constricted area and the shear flow downstream disperses the particles into aerosol form. The Venturi was powered using pre-filtered compressed air at 5, 10 and 12 psi. Nozzle pressure was monitored using a pressure gauge and was recorded initially. The airflow through the chamber was adjusted to insure adequate mixing and uniform concentration of the test article. The chamber atmosphere was exhausted through a tube from the bottom of the chamber, thereby insuring that the aerosol was drawn over the animals' breathing zone. The exhaust air was passed through filters before entering into a rotameter and vacuum pump.

EXPERIMENTAL DESIGN (continued)

Concentration (Appendix 3

The target concentration was determined prior to exposure by determining the best flow rate for generating the desired concentration.

In order to calculate the concentration gravimetrically, the total solid was determined prior to exposure by drying a preweighed sample of the test article for two minutes, reweighing and calculating the total solid:

$$\frac{\text{Final weight}}{\text{Initial weight}}$$

During the exposure, chamber air was drawn over preweighed filters. The filters were removed and reweighed. The actual concentration of the test article was calculated based on the total solid, the amount of test article collected and the air flow through the chamber. The average concentration was reported.

Particle Size Measurements (Appendix 4)

Mass mean aerodynamic diameter (MMAD) was calculated pretest. An 8 stage Andersen cascade impactor was used to determine particle size. Air was drawn through the impactor for 30 seconds at the 1.6 and 2.3 mg/l exposure and for one minute at the 1.9 mg/l exposure. The impactor filter paper collection stages were weighed before and after the air sampling to determine the mass collected at each filter paper collection stage. The MMAD was determined graphically using three cycle logarithmic probit paper. The geometric standard deviation was calculated. A pretest MMAD of 4 microns or less was required to ensure that the particles generated during exposure were in the respirable range. Particle size measurements were recorded four times during the exposure period. The average particle size was calculated.

Type and Frequency of Observations

In Vivo - Animals were observed at approximately 30 minute intervals during exposure, at one hour post exposure and once daily thereafter for 14 days for signs of toxicity and pharmacological effects. The animals were observed twice daily for mortality. Body weights were recorded pretest, weekly, at death and at termination in the survivors.

Post Mortem: All animals were examined for gross pathology. Abnormal tissues were preserved in 10% buffered formalin for possible future microscopic examination.

EXPERIMENTAL DESIGN (continued)

Analysis of Data

Determination of a Poisonous Material: A poisonous material as defined in 49 CFR 173.132(a) is a material, other than a gas, which is known to be so toxic to humans as to afford a hazard to health during transportation, or which in the absence of adequate data on human toxicity is presumed to be toxic to humans because it falls within the following category when tested on laboratory animals.

A dust or a mist with an LC_{50} for acute inhalation toxicity of not more than 10 mg/l.

Assignment of Packing Group and Hazard Zones:

PACKING GROUP	LC_{50} (mg/l)
I	<0.5
II	>0.5<2.0
III	>2.0<10.0

Retention of Data

The raw data is filed at MB Research by project number. The final report is filed at MB Research by sponsor name and MB project number. The preserved tissues are stored at MB Research by sponsor name and MB project number. The sponsor will be contacted for final disposition of the tissues upon submission of the report.

The test article will be returned to the sponsor following submission of the report.

Amendment to the Protocol

There were no amendments to the protocol.

Study Title : Inhalation Toxicity in Rats
Project # : MB 98-7240.05
Test Article : MATRIMID 5292A US
Batch #AG86890010
Protocol : 318E-01

RESULTS & DISCUSSION

1. **LC_{50}**

The LC_{50} is approximately 1.9 mg/l. The test article is assigned to Packing Group II.

2. **Mortality**

Mortality response to the inhalation exposures was:

Actual Concentration in mg/l	Exposure Period	# Exposed M/F	# Dead M/F
1.6	1 hour	5/5	1/0
1.9	1 hour	5/5	4/5
2.3	4 hours	5/5	4/1

3. **Systemic Observations, Body Weights and Necropsy Observations (Tables 1, 2 and 3)**

1.6 mg/l - One hour exposure - Nine of ten animals survived the one hour 1.6 mg/l exposure. One male died on day 1 with predeath physical signs of dyspnea, coating of the fur with test material and closed eyes. Necropsy revealed abnormalities of the lungs, eyes, liver, kidneys, adrenals and gastrointestinal tract, as well as wetness of the nose/mouth area.

Physical signs of abnormal licking, coating of the fur with test article and closed eyes were noted during the exposure period in the survivors. Instances of dyspnea and emaciation were noted in survivors during the remainder of the study. Body weight changes of survivors were normal in 5/9 survivors. Instances of weight loss were noted in four animals. Necropsy results of survivors were normal.

1.9 mg/l - One hour exposure - Five animals survived the one hour 1.9 mg/l exposure. Four males and one female died within 2 days of the exposure. Predeath physical signs included lethargy, ataxia, dyspnea, chromodacryorrhea, closed eyes, wetness and red staining of the nose/mouth area, and coating of the fur with test article. Necropsy revealed abnormalities of the lungs, nasal turbinates, eyes, pleural cavity, liver, kidneys and gastrointestinal tract, as well as red staining and wetness of the nose mouth area.

Physical signs noted in survivors included chromodacryorrhea, chromorhinorrhea, dyspnea, lethargy, piloerection, emaciation, tremors, sagging eyelids, coating of the fur with test article, closed eyes, hunched posture and wetness or red staining of the nose/mouth area. Body weight changes were normal in 4/5 survivors. One female lost weight during the study. Necropsy results were normal in 3/5 survivors and lung abnormalities were noted in two animals.

RESULTS & DISCUSSION (cont'd)

2.3 mg/l - Four hour exposure - One animal survived the four hour 2.3 mg/l exposure. Four males and five females died by day 1 with predeath physical signs of dyspnea, tremors, lethargy, sagging eyelids, piloerection, chromodacryorrhea, wetness and red staining of the nose/mouth area, fur coated with test article, closed eyes and abnormal climbing. Necropsy revealed abnormalities of the lungs, nasal turbinates, eyes, liver, adrenals and gastrointestinal tract, as well as wetness of the nose/mouth and anogenital areas.

Physical signs of dyspnea, lethargy, sagging eyelids, ataxia, flaccid muscle tone, red staining of the nose/mouth area, coating of the fur with test article and closed eyes, were noted in the surviving animal. Body weight changes and necropsy results of the survivors were normal.

CONCLUSION

The LC_{50} is approximately than approximately 1.9 mg/l. The test article is assigned to Packing Group II.

FINAL REPORT

Approved by: Daniel R. Cerven, M.S. Study Director — Date 1 Dec 99

Study Title	:	**Inhalation Toxicity in Rats**
Project #	:	**MB 98-7240.05**
Test Article	:	**MATRIMID 5292A US Batch #AG86890010**
Protocol	:	**318E-01**

Table 1: Systemic Observations

TOXICITY CODE

B	=	Lethargy
C	=	Flaccid
E	=	Ataxia
F	=	Piloerection
J	=	Chromodacryorrhea
M	=	Dyspnea
O	=	Tremors
Q	=	Sagging eyelids
S	=	Chromorhinorrhea
W	=	Appears emaciated
Z	=	Dead
1	=	eyes closed
2	=	nose/mouth area wet
3	=	nose/mouth area stained red
4	=	fur coated with test article
8	=	appeared to be licking inside of mouth
9	=	hunched position
10	=	animal climbing on side of cage

Study Title : Inhalation Toxicity in Rats
Project # : MB 98-7240.05
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Protocol : 318E-01

Table 1: Systemic Observations (continued)

Concentration: 1.6 mg/l (One Hour Exposure)

TIME PERIODS	ANIMAL # / SEX									
	1/M	2/M	3/M	4/M	5/M	6/F	7/F	8/F	9/F	10/F
Day 0: 20 Minutes	1,4	1,4	1,4	1,4	1,4	1,4	1,4	1,4	1,4	1,4
Day 0: 45 Minutes	1,4	1,4	1,4,8	1,4	1,4	1,4	1,4,8	1,4	1,4	1,4
Day 0: Hour 1	M	M					M	M		
Day 1		$Z^{(248g)}$					M	M		M
Day 2						W				
Day 3										
Day 4										
Day 5										
Day 6										
Day 7										
Day 8										
Day 9										
Day 10										
Day 11										
Day 12										
Day 13										
Day 14										

No entry indicates animal appeared normal at that observation period. Systemic observation code is on page preceding systemic observation tables.

Study Title : Inhalation Toxicity in Rats
Project # : MB 98-7240.05
Test Article : MATRIMID 5292A US Batch #AG86890010
Protocol : 318E-01

Table 1: Systemic Observations (continued)

Concentration: 1.9 mg/l (One Hour Exposure)

TIME PERIODS	ANIMAL # / SEX									
	21/M	22/M	23/M	24/M	25/M	26/F	27/F	28/F	29/F	30/F
Day 0: 18 Minutes	1,4	1,4,M	1,4	1,4	1,4,M	1,4,M	1,4	1,4,M	1,4,M	1,4,M
Day 0: 44 Minutes	1,4,M	1,4,M	1,4,M	1,4,M	1,4,M	1,2,4,9,M	1,4,M	1,4,M	Z	1,4,M
Day 0: Hour 1	M,4	J,S,M,2,4	M,2,4	M,4	M,4	M,B,2,4	M,4	M,4	Z	4
Day 1	M,B,E,3, $Z^{(217g)}$	M,J,S	B,M,J,3	$Z^{(219g)}$	$Z^{(216g)}$	O,M,B,Q,3	M,3	S,J,M		
Day 2		M,J,S	$Z^{(192g)}$			M,B,Q,2,3	M,B,3	S,J,M,2,3		
Day 3		M				B,E,M,S,F, W,2,3	M			
Day 4		M				B,E,M,S,F, W,2,3	M,F			
Day 5		M				S,F,W,3	F			
Day 6		M				F,S,W,3	F			
Day 7		M				F,W				
Day 8										
Day 9										
Day 10										
Day 11						S				
Day 12						S				
Day 13						S				
Day 14										

No entry indicates animal appeared normal at that observation period. Systemic observation code is on page preceding systemic observation tables.

Study Title : Inhalation Toxicity in Rats
Project # : MB 98-7240.05
Test Article : MATRIMID 5292A US Batch #AG86890010
Protocol : 318E-01

Table 1: Systemic Observations (continued)

Concentration: 2.3 mg/l (Four Hour Exposure)

TIME PERIODS	ANIMAL #/SEX									
	11/M	12/M	13/M	14/M	15/M	16/F	17/F	18/F	19/F	20/F
Day 0: 30 Minutes	1,4	1,4	1,4	1,4	1,4,10	1,4	1,4	1,4	1,4	1,4
Day 0: 67 Minutes	1,4	1,4	1,4	1,4	1,4	1,4	1,4	1,4	1,4	1,4
Day 0: 135 Minutes	M,1,4	M,1,4	M,1,4	M,1,4	M,1,4	M,1,4,10	M,1,4	M,1,4	M,1,4	M,1,4
Day 0: 202 Minutes	M,1,4	M,1,4	M,O,1,4	M,1,4	M,1,4	M,O,1,4	M,1,4	M,1,4	M,1,4	M,1,4
Day 0: Hour 1	M,B,Q,3,4	Z	B,M,F,Q,2,4,Z(255g)	B,M,Q,2,4	M,Q,3,4	Q,B,M,3,4	M,B,J,F,2,4	B,M,2,4	Q,B,M,O,2,4	M,2,4
Day 1	Z(208g)			Z(230g)	Q,B,E,C,M,3,4	Z(209g)	Z(213g)	Z(246g)	Z(236g)	Z(215g)
Day 2					Q,B,E,C,M,3,4					
Day 3					M,3,4					
Day 4					M,3					
Day 5					M,3					
Day 6					M					
Day 7					M					
Day 8					M					
Day 9					M					
Day 10										
Day 11										
Day 12										
Day 13										
Day 14										

No entry indicates animal appeared normal at that observation period. Systemic observation code is on page preceding systemic observation tables.

Study Title : Inhalation Toxicity in Rats
Project # : MB 98-7240.05
Test Article : MATRIMID 5292A US
Batch #AG86890010
Protocol : 318E-01

Table 2: Body Weights

Concentration: 1.6 mg/l (One Hour Exposure)

An.#	Sex	Day 0	Day 7	Day 14
1	M	267	300	340
2	M	274		
3	M	249	290	335
4	M	253	283	320
5	M	260	297	343
	MEAN	261	293	335
	S.D.	10.2	7.6	10.2
	#	5	4	4
6	F	247	256	266
7	F	265	278	276
8	F	273	265	259
9	F	259	262	277
10	F	264	261	264
	MEAN	262	264	268
	S.D.	9.6	8.3	7.8
	#	5	5	5

Concentration: 1.9 mg/l (One Hour Exposure)

An.#	Sex	Day 0	Day 7	Day 14
21	M	244		
22	M	266	291	352
23	M	226		
24	M	248		
25	M	235		
	MEAN	244		
	S.D.	15.0		
	#	5		
26	F	244	209	230
27	F	234	244	251
28	F	250	240	253
29	F	222		
30	F	225	233	240
	MEAN	235	232	244
	S.D.	12.0	15.7	10.7
	#	5	4	4

No entry indicates animal died before observation period.

Study Title : Inhalation Toxicity in Rats
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Table 2: Body Weights (continued)

Concentration: 2.3 mg/l (Four Hour Exposure)

An. #	Sex	Day 0	Day 7	Day 14
11	M	230		
12	M	266		
13	M	279		
14	M	251		
15	M	257	261	328
	MEAN	257		
	S.D.	18.2		
	#	5		
16	F	229		
17	F	233		
18	F	273		
19	F	260		
20	F	236		
	MEAN	246		
	S.D.	19.3		
	#	5		

No entry indicates animal died before observation period.

Study Title : Inhalation Toxicity in Rats
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Table 3: Necropsy Observations

Concentration: 1.6 mg/l (One Hour Exposure)

ANIMAL NUMBER/SEX	1/M	2/M	3/M	4/M	5/M	6/F	7/F	8/F	9/F	10/F
OBSERVATION Death/Sacrifice	S	D	S	S	S	S	S	S	S	S
Normal	X		X	X	X	X	X	X	X	X
Eyes - opaque		2								
Nose/mouth - wet and bubbly		1								
Lungs - darker than normal		3								
Lungs - red areas		3								
Nasal turbinates		X								
Liver - pale areas		2								
Kidneys - pale		1								
Stomach - distended with gas		1								
Adrenals - darker than normal		1								
Intestines - red areas		1								
Intestines - yellow areas		1								
Intestines - lower one distended with gas		2								
Cecum - distended with gas		1								

CODES:
D = death
S = sacrifice
X = observed
1= slight or scattered
2= moderate or few
3= pronounced or many

Study Title : Inhalation Toxicity in Rats
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Table 3: Necropsy Observations

Concentration: 1.9 mg/l (One Hour Exposure)

ANIMAL NUMBER/SEX	21/M	22/M	23/M	24/M	25/M	26/F	27/F	28/F	29/F	30/F
OBSERVATION Death/Sacrifice	D	S	D	D	D	S	S	S	D	S
Normal						X		X		X
Eyes - opaque			2	2	2					
Nose/mouth - stained red	2		1	1						
Nose/mouth - wet	1			2	1					
Lungs - inflated									2	
Lungs - darker than normal	3	2	3	3	2		1			
Lungs - red areas	3	2	3	3	3		2			
Nasal turbinates	X		1R	1R	1R				X	
Pleural cavity - excess fluid	2		2							
Liver - pale areas	1		1		1				1	
Liver - darker than normal			1							
Kidney - pale	2		1		2					
Intestines - red areas	1		1							
Intestines - yellow areas	2		3	2	1					
Intestines - distended with gas					2					

CODES: D = death; S = sacrifice; X = observed; 1= slight or scattered; 2= moderate or few; 3= pronounced or many; R= redness

Study Title : Inhalation Toxicity in Rats
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Table 3: Necropsy Observations

Concentration: 2.3 mg/l (Four Hour Exposure)

ANIMAL NUMBER/SEX	11/M	12/M	13/M	14/M	15/M	16/F	17/F	18/F	19/F	20/F
OBSERVATION Death/Sacrifice	D	D	D	D	S	D	D	D	D	D
Normal					X					
Eyes - opaque	2	2		2		2				
Eye - right eye opaque			2							
Nose/mouth - wet	2	2	2	2		1	2	2	2	2
Anogenital area - wet			1							
Lungs - fluid filled	3	2	2	2		2	3	3	3	3
Lungs - darker than normal	3	3	3	3		3	3	3	3	3
Lungs - red areas	3	3	3	3		3	3	3	3	3
Nasal turbinates	1*	2*	2*	2*		2*	3*	2*	1*	2*
Liver - pale areas								2	1	
Liver - darker than normal	1		2	2		2	2	2	2	2
Adrenals - darker than normal		1								
Stomach - red			1							
Intestines - red areas	2	2	2	3		3	3	3	3	3
Intestines - distended with mucus				2		2	3	3	2	3
Intestines - yellow areas	2			2		2	3	2	1	2

CODES: D = death; S = sacrifice; X = observed
1= slight or scattered; 2= moderate or few; 3= pronounced or many
*= red with white material present

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Appendix 1: Chamber Conditions

Concentration 1.6 mg/l (One Hour Exposure)

Time (minutes)	Airflow l/min	Temperature °C	Negative Pressure inches H_2O	Relative Humidity of Air Entering Chamber %
20	25	21.9	20	50
45	25	22.0	20	50

Concentration 1.9 mg/l (One Hour Exposure)

Time (minutes)	Airflow l/min	Temperature °C	Negative Pressure inches H_2O	Relative Humidity of Air Entering Chamber %
18	25	20	20	55
44	25	20	20	55

Concentration 2.3 mg/l (Four Hour Exposure)

Time (minutes)	Airflow l/min	Temperature °C	Negative Pressure inches H_2O	Relative Humidity of Air Entering Chamber %
35	25	19.8	20	50
65	25	20.4	20	50
133	25	20.9	20	48
200	25	20.9	20	46

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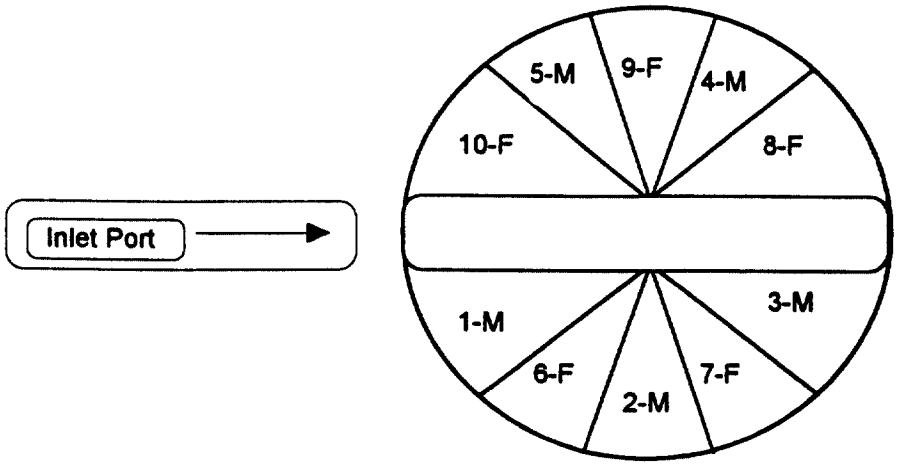
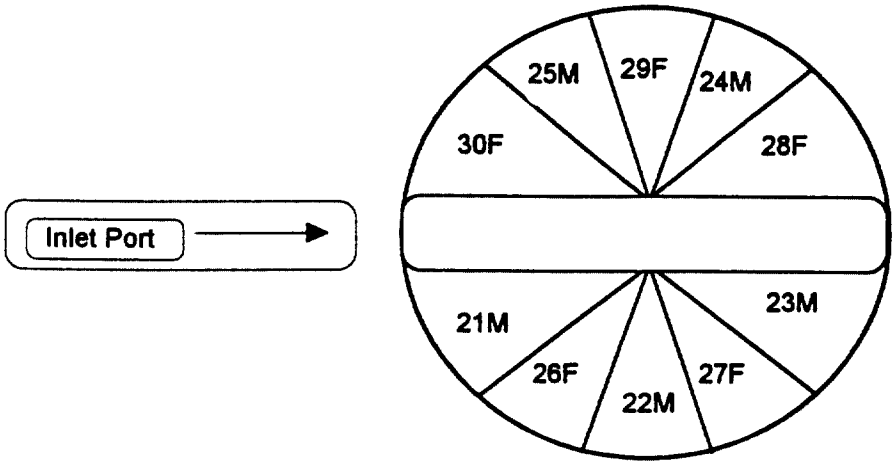
Appendix 2: Position of Rats in Exposure Chamber

Concentration: 1.6 mg/l (One Hour Exposure)

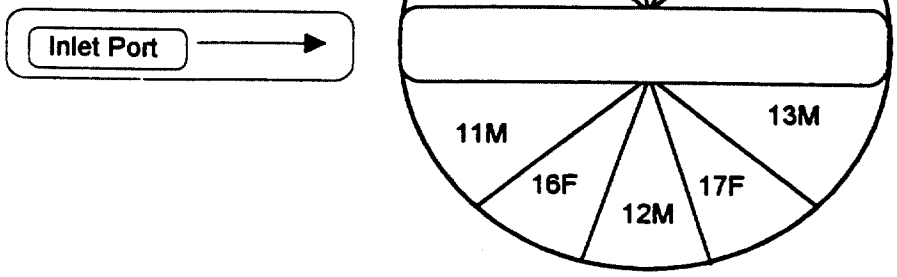


Concentration: 1.9 mg/l (One Hour Exposure)



Appendix 2: Position of Rats in Exposure Chamber (continued)

Concentration: 2.3 mg/l (Four Hour Exposure)



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Appendix 3: Chamber Concentrations

Total Solid Calculation

Sample #	Tare Weight (g)	Test Article Volume (g)	Test Article + Tare Initial Weight (g)	Test Article + Tare Final Weight (g)	Final Weight/ Initial Weight
1	0.0905	0.1	0.1920	0.1917	1.00
2	0.0910	0.1	0.1927	0.1925	1.00
3	0.0907	0.1	0.1921	0.1919	1.00
				Mean	1.00
				SD	0.00
				n	3

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Appendix 3: Concentration Determination (continued)

Concentration: 1.6 mg/l (One Hour Exposure)

Sample #	Measured Test Article (g)	Total Solid	Total Test Article* (g)	Air Volume Liters	Total Concentration (mg/l)
1	0.0083	1.00	0.0083	6	1.4
2	0.0220	1.00	0.0220	6	3.7
3	0.0038	1.00	0.0038	6	0.63
4	0.0102	1.00	0.0102	6	1.7
5	0.0040	1.00	0.0040	6	0.67
				Mean	1.6
				SD	1.3
				n	5

*Total Test Article = Measured Test Article/Total Solid

Concentration: 1.9 mg/l (One Hour Exposure)

Sample #	Measured Test Article (g)	Total Solid	Total Test Article* (g)	Air Volume Liters	Total Concentration (mg/l)
1	0.0114	1.00	0.0114	6	1.9
2	0.0079	1.00	0.0079	6	1.3
3	0.0139	1.00	0.0139	6	2.3
4	0.0122	1.00	0.0122	6	2.0
				Mean	1.9
				SD	0.42
				n	4

*Total Test Article = Measured Test Article/Total Solid

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Appendix 3: Concentration Determination (continued)

Concentration: 2.3 mg/l (Four Hour Exposure)

Sample #	Measured Test Article (g)	Total Solid	Total Test Article* (g)	Air Volume Liters	Total Concentration (mg/l)
1	0.0123	1.00	0.0123	6	2.1
2	0.0195	1.00	0.0195	6	3.3
3	0.0143	1.00	0.0143	6	2.4
4	0.0057	1.00	0.0057	6	1.0
5	0.0113	1.00	0.0113	6	1.9
6	0.0133	1.00	0.0133	6	2.2
7	0.0121	1.00	0.0121	6	2.0
8	0.0237	1.00	0.0237	6	4.0
9	0.0160	1.00	0.0160	6	2.7
10	0.0063	1.00	0.0063	6	1.1
				Mean	2.30
				SD	0.91
				n	10

*Total Test Article = Measured Test Article/Total Solid

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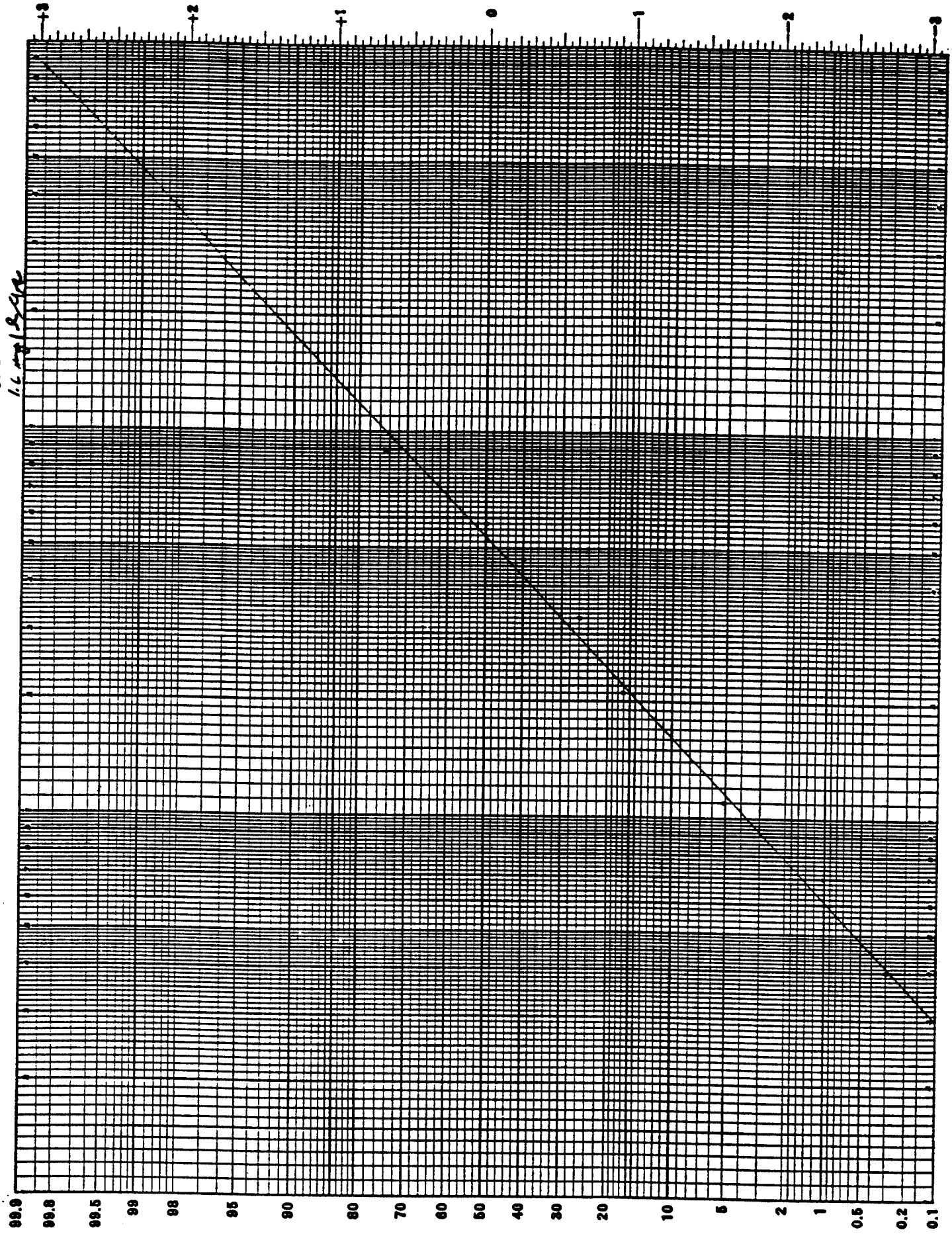
Appendix 4: Particle Size

Concentration: 1.6 mg/l Run # 1 (One Hour Exposure)

Effective Cut-off Diameter Micrometers	Initial Filter Weight (g)	Final Filter Weight (g)	Net Collected (g)	% of Total Weight in Size Range	Cumulative % Less Than Size Range
10.0	374.53	374.54	0.01	25.1	100.0
9.0	125.15	125.16	0.01	25.1	74.9
5.8	0.3312	0.3351	0.0039	9.8	49.8
4.7	0.3297	0.3352	0.0055	13.8	40.0
3.3	0.3634	0.3670	0.0036	9.0	26.2
2.1	0.3631	0.3673	0.0042	10.6	17.2
1.1	0.3621	0.3643	0.0022	5.5	6.6
0.7	0.3601	0.3604	0.0003	0.8	1.1
0.4	0.3657	0.3657	0.0000	0.0	0.3
0	0.3653	0.3654	0.0001	0.3	0.3
		Total:	0.0398		

16% Diameter - Micrometers =	2.10
50% Diameter - Micrometers =	5.37
84% Diameter - Micrometers =	13.50
Mass Mean Aerodynamic Diameter (MMAD) - Micrometers =	5.37
Geometric Standard Deviation = Square root of 84%/16% =	2.54
84%/50% =	2.51
50%/16% =	2.56


-3
-2
-1
0
1
2
3
99.9
99.8
99.5
99
98
95
90
80
70
60
50
40
30
20
10
5
2
1
0.5
0.2
0.1

Study Title : **Inhalation Toxicity in Rats**
Project # : **MB 98-7240.05**
Test Article : **MATRIMID 5292A US**
Batch #AG86890010
Protocol : **318E-01**

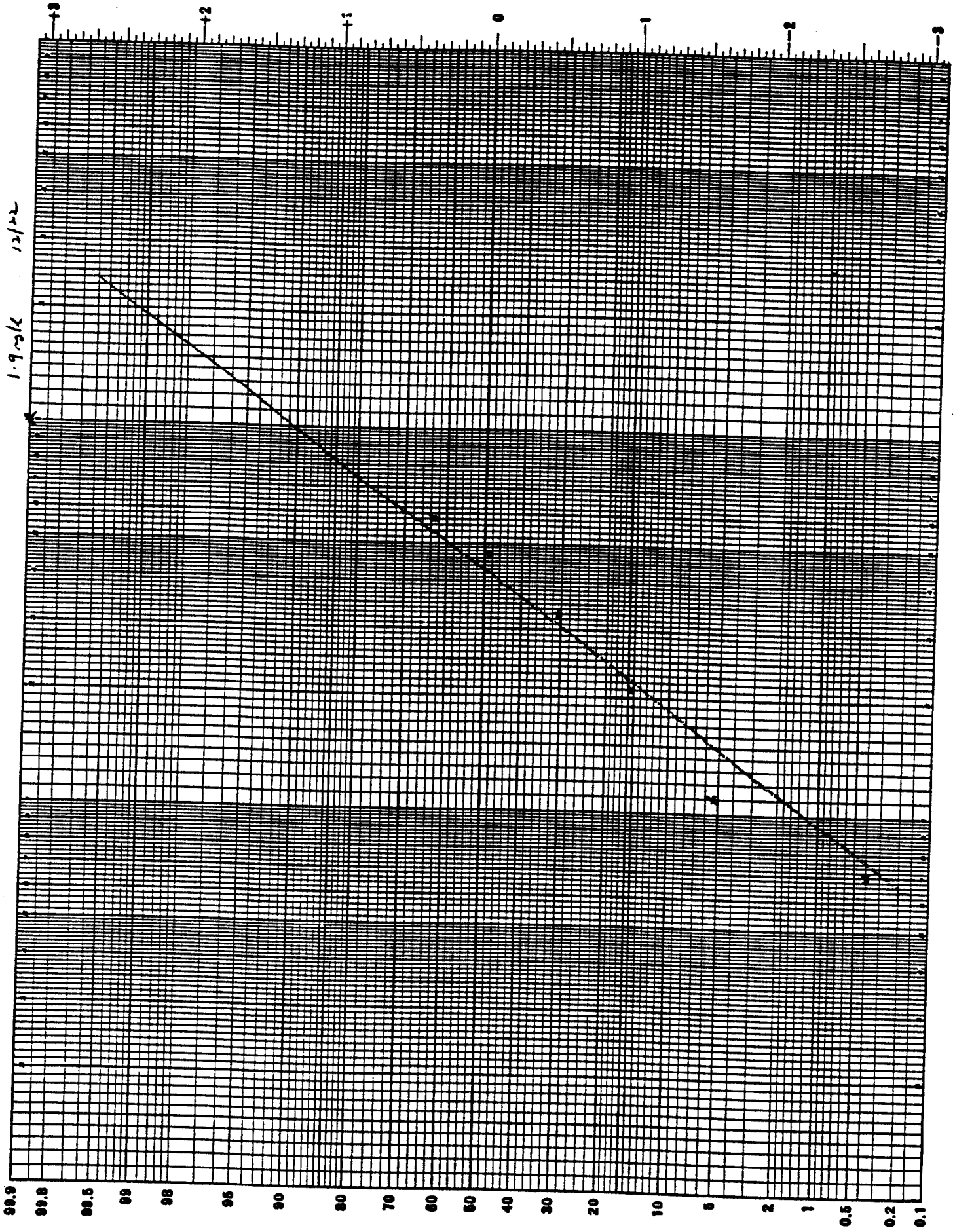
Appendix 4: Particle Size (continued)

Concentration: 1.9 mg/l Run # 1 (One Hour Exposure)

Effective Cut-off Diameter Micrometers	Initial Filter Weight (g)	Final Filter Weight (g)	Net Collected (g)	% of Total Weight in Size Range	Cumulative % Less Than Size Range
10.0	374.55	374.56	0.0100	36.5	99.9
9.0	125.17	125.16	-0.0100	NA	NA
5.8	0.3244	0.3283	0.0039	14.2	63.4
4.7	0.3259	0.3309	0.0050	18.2	49.2
3.3	0.3640	0.3676	0.0036	13.1	31.0
2.1	0.3626	0.3660	0.0034	12.4	17.9
1.1	0.3623	0.3637	0.0014	5.1	5.5
0.7	0.3664	0.3665	0.0001	0.4	0.4
0.4	0.3629	0.3622 a	-0.0007	NA	NA
0	0.3688	0.3688	0.0000	0.0	0.0
		Total:	0.0274		

16% Diameter - Micrometers =	2.24
50% Diameter - Micrometers =	4.30
84% Diameter - Micrometers =	8.20
Mass Mean Aerodynamic Diameter (MMAD) - Micrometers =	4.30
Geometric Standard Deviation = Square root of 84%/16% =	1.91
84%/50% =	1.91
50%/16% =	1.92

a = no test article visible on filter


98-7240.05 BV
Matrimid RUN# 1
1.9 mil 12/22
+3
+2
+1
0
-1
-2
-3
99.9
99.8
99.5
99
98
95
90
80
70
60
50
40
30
20
10
5
2
1
0.5
0.2
0.1

Study Title : Inhalation Toxicity in Rats
Project # : MB 98-7240.05
Test Article : MATRIMID 5292A US
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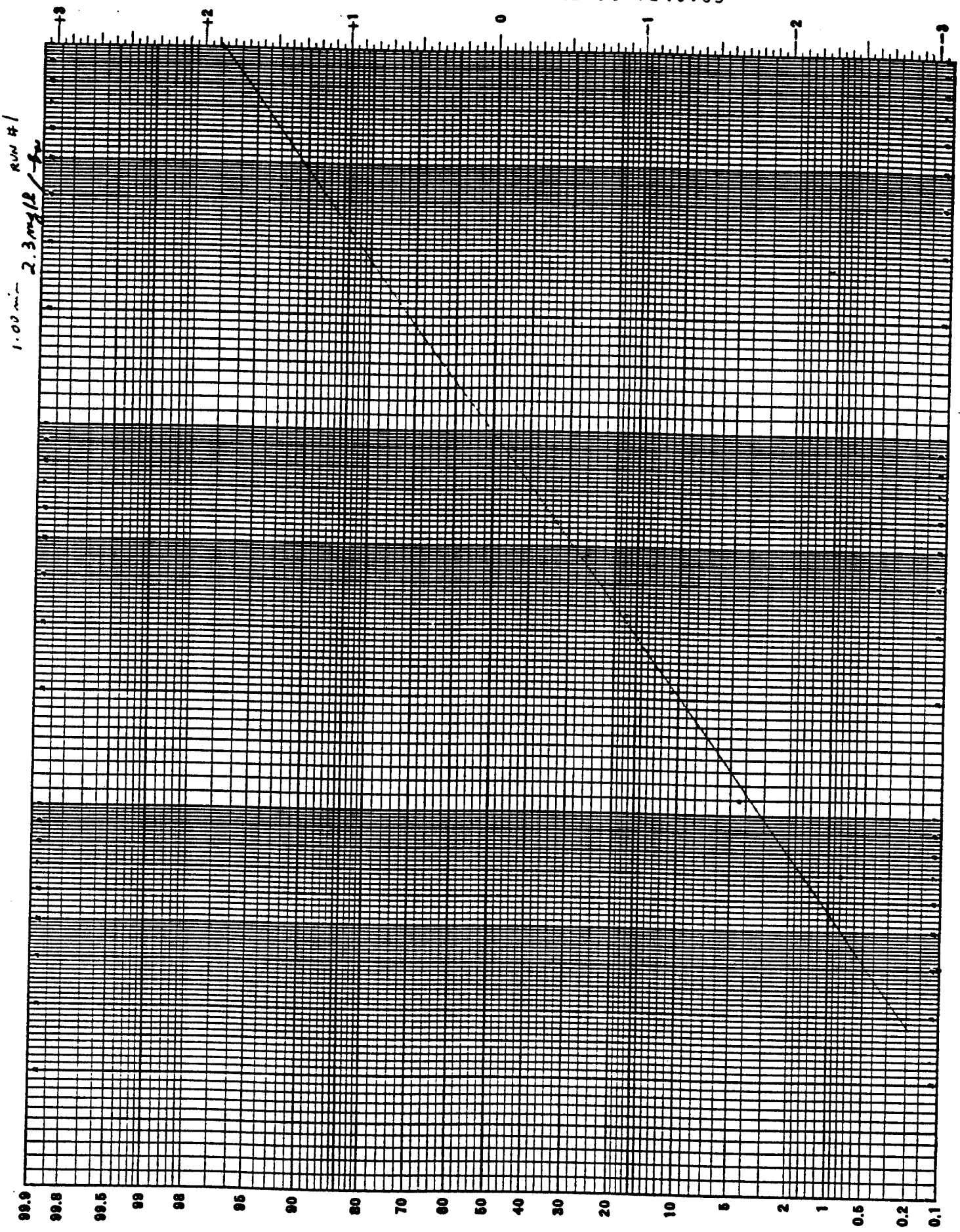
Appendix 4: Particle Size (continued)

Concentration: 2.3 mg/l Run # 1 (Four Hour Exposure)

Effective Cut-off Diameter Micrometers	Initial Filter Weight (g)	Final Filter Weight (g)	Net Collected (g)	% of Total Weight in Size Range	Cumulative % Less Than Size Range
10.0	374.56	374.61	0.0500	55.6	100.0
9.0	125.16	125.17	0.0100	11.1	44.4
5.8	0.3284	0.3349	0.0065	7.2	33.3
4.7	0.3234	0.3310	0.0076	8.5	26.1
3.3	0.3655	0.3717	0.0062	6.9	17.6
2.1	0.3662	0.3719	0.0057	6.3	10.7
1.1	0.3655	0.3687	0.0032	3.6	4.4
0.7	0.3695	0.3701	0.0006	0.7	0.8
0.4	0.3624	0.3625	0.0001	0.1	0.1
0	0.3623	0.3623	0.0000	0.0	0.0
		Total:	0.0899		

16% Diameter - Micrometers =	2.90
50% Diameter - Micrometers =	9.90
84% Diameter - Micrometers =	34.00
Mass Mean Aerodynamic Diameter (MMAD) - Micrometers =	9.90
Geometric Standard Deviation = Square root of 84%/16% =	3.42
84%/50% =	3.43
50%/16% =	3.41


98 - 7240.05
MATRIMO 52924 US
1.00 min 2.3mg/12 hr
RUN #1
12/11/98
+3
+2
+1
0
-1
-2
-3
99.9
99.8
99.5
99
98
95
90
80
70
60
50
40
30
20
10
5
2
1
0.5
0.2
0.1

Study Title : Inhalation Toxicity in Rats
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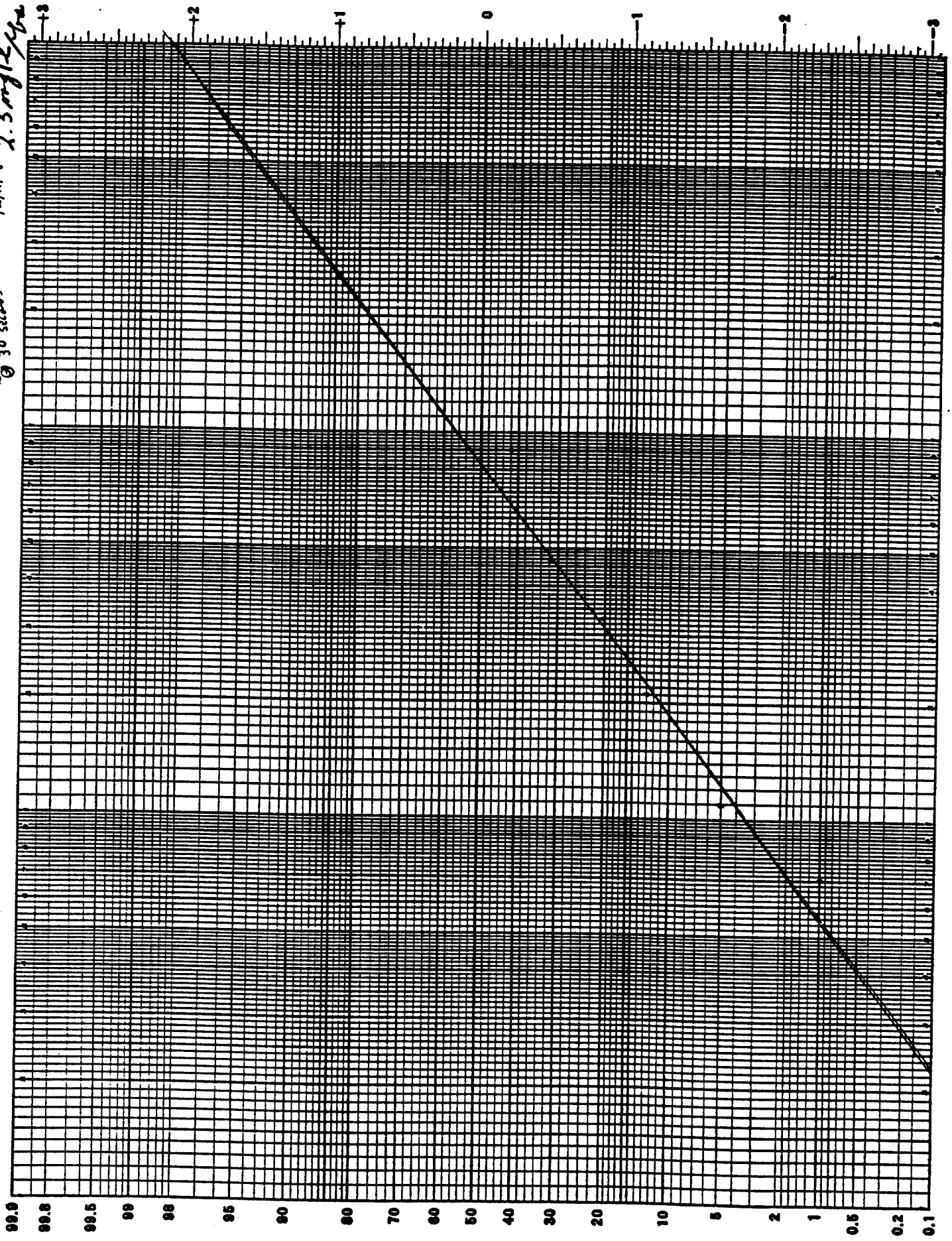
Appendix 4: Particle Size (continued)

Concentration: 2.3 mg/l Run # 2 (Four Hour Exposure)

Effective Cut-off Diameter Micrometers	Initial Filter Weight (g)	Final Filter Weight (g)	Net Collected (g)	% of Total Weight in Size Range	Cumulative % Less Than Size Range
10.0	374.56	374.60	0.0400	58.0	100.0
9.0	125.16	125.16	0	0	42.0
5.8	0.3236	0.3304	0.0068	9.9	42.0
4.7	0.3254	0.3335	0.0081	11.7	32.1
3.3	0.3615	0.3666	0.0051	7.4	20.4
2.1	0.3661	0.3714	0.0053	7.7	13.0
1.1	0.3649	0.3679	0.0030	4.3	5.3
0.7	0.3688	0.3695	0.0007	1.0	1.0
0.4	0.3615	0.3615	0.0000	0.0	0.0
0	0.3610	0.3610	0.0000	0.0	0.0
		Total:	0.0690		

16% Diameter - Micrometers =	2.60
50% Diameter - Micrometers =	8.30
84% Diameter - Micrometers =	27.00
Mass Mean Aerodynamic Diameter (MMAD) - Micrometers =	8.30
Geometric Standard Deviation = Square root of 84%/16% =	3.22
84%/50% =	3.25
50%/16% =	3.19


98-7240.05
Marianna Sand US
@ 30 seconds
Run # 2
pw
12/11/98
2.3 mg/L/psi
-3
-2
-1
0
1
2
3
99.9
99.8
99.5
99
98
95
90
80
70
60
50
40
30
20
10
5
2
1
0.5
0.2
0.1

Study Title : **Inhalation Toxicity in Rats**
Project # : **MB 98-7240.05**
Test Article : **MATRIMID 5292A US**
Batch #AG86890010
Protocol : **318E-01**

QUALITY ASSURANCE EVALUATION

The Quality Assurance Unit has inspected an in-life phase of this study, audited the raw data and the report and determined that the methods and results contained herein accurately reflect the raw data. No deviations from the approved protocol or Standard Operating Procedures were made without proper authorization and documentation. A summary of the compliance inspections is presented below.

Date of Inspection	Phase	Performed By	Date Findings Reported to	
			Mgmt.	Sty. Dir.
12/09/98	Necropsy	Kathleen M. Dalton	3/02/99	3/01/99
01/18/99	Raw data audit	Kathleen M. Dalton	3/02/99	3/01/99
02/09/99	Draft report audit	Kathleen M. Dalton	3/02/99	3/01/99
03/01/99	Final report audit	Betty Salyer	3/02/99	3/01/99

Bonnie W. Cerven 3-2-99
Bonnie W. Cerven, RQAP Date
Director, Regulatory Compliance